DETAILED ACTION

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on January 14, 2009 has been entered.

2. The proposed supplemental amendment filed on March 10, 2009 has not been entered because it is unsigned.

3. Claims 1-42 have been cancelled.

Claims 43-45, 50-52, 58, and 60 have been amended.

Claims 58-60 remain withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on September 20, 2007.

4. Claims 43-57 and 61-66 are under examination.

5. The species election between the sequences, as set forth in the Office action mailed on April 23, 2007, has been reconsidered. Claim 48, 51, 52, 55-57, and 65 directed to non-elected sequences are no longer withdrawn from consideration because the sequences are overlapping transcripts in a genomic region that is only transcribed in B-CLL patients with poor prognosis.

In view of the above noted withdrawal of the species election, applicant is advised that if any claim presented in a continuation or divisional application is anticipated by, or includes all the limitations of, a claim that is allowable in the present application, such claim may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application.

Once a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. See *In re Ziegler*, 443 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

6. The following office action contains NEW GROUNDS of Rejection.

Information Disclosure Statement

7. The information disclosure statement (IDS) submitted on December 23, 2008 has been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this office action.

Rejections Withdrawn

8. The rejection of claims 43-47, 49, 50, 53, and 54 under 35 U.S.C. 112, first paragraph as lacking enablement is withdrawn in view of applicant's declaration and the new grounds of rejection below.

NEW GROUNDS of Rejection

Claim Objections

9. Claim 62 is objected to because of the following informalities: The claim is a duplicate of claim 53. Appropriate correction is required.

10. Claims 55-57 are objected to because of the following informalities: The claims depend from canceled claim 42. Appropriate correction is required.

11. Claim 50 objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 50 is not further limiting with respect to SEQ ID No. 13 in the base claims because SEQ ID No. 13 represent exon 3 and the sequences in claim 50 are larger transcripts which do not each contain exon 3.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 43-57 and 61-66 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for diagnosing a subtype of B-CLL with poor prognosis by detecting mRNA transcripts using primers to detect the exon 2/exon 3 splice junction or using SEQ ID Nos. 13, 15-17 as probes, does not reasonably provide enablement for diagnosing a subtype of B-CLL by detecting SEQ ID Nos. 13 or 15-17. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described by the court in In re Wands, 8 USPQ2d 1400 (CAFC 1988).

> Wands states on page 1404,
> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to detecting SEQ ID Nos. 13 and 15-17 in patients having a poor prognosis of B-CLL. The specification discloses SEQ ID Nos. 13 and 15-

17 as being exons 1-3 and a coding sequence respectively. The sequences represent DNA regions of the larger genomic sequence SEQ ID Nos. 1 and 5. The specification discloses the sequences of SEQ ID Nos. 13 and 15-17 were used as probes in northern blots to detect transcription in this genomic region, i.e., transcripts which “comprise" these exon sequences. The specification does not disclose detection of DNA in diagnosing B-CLL. The specification does not disclose detection of RNA transcripts comprising only SEQ ID Nos. 13 and 15-17.

Buhl, et al. (Blood, 2006. vol. 107, pages 2904-2911, as cited on the IDS filed December 23, 2008) teach detection of transcription products from the CLLU1 region (SEQ ID No. 1) by RT-PCR and northern blots as being indicative of a poor prognosis of B-CLL. Buhl, et al. teach a number of differentially spliced transcripts in this genomic region (see figure 2). Buhl, et al. do not teach detection of DNA being indicative of poor prognosis of B-CLL. Josefsson, et al. (Blood, 2007. Vol. 109, pages 4973-4979, as cited on the IDS filed December 23, 2008) teach RT-PCR detection of transcripts from the CLLU1 region in patients with poor prognosis of B-CLL.

While the shorter exon sequences can be detected, detection of just the exon sequences would not provide a predictable nexus or link between detection and a poor prognosis. The specification discloses isolation of RNA to detect transcripts (example 3). The specification indicates the criticality of the presence of the complete transcripts. The specification discloses the correlation with a poor prognosis of B-CLL and the detection of complete transcripts and the absence of a correlation between the

detection of just SEQ ID Nos. 13, 15, 16, or 17 and a correlative poor prognosis (page 36 and figures 3 and 10).

There is insufficient evidence or nexus that would lead the skilled artisan to predict the ability to diagnosis a poor prognosis of B-CLL by detecting SEQ ID Nos. 13 and 15-17. The specification does not teach detection of DNA in determining a poor prognosis of B-CLL. The specification does not teach detection of RNA transcripts consisting of SEQ ID Nos. 13 or 15-17.

In view of the lack of the predictability of the art to which the invention pertains undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for diagnosing a poor prognosis of B-CLL, commensurate in scope with the claimed invention.

Conclusion

14. No claims are allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANNE M. GUSSOW whose telephone number is (571)272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow
March 23, 2009

/David J Blanchard/
Primary Examiner, Art Unit 1643